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Jan 20, 1988

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TITLE: Single-component tissue adhesive and method for producing same.

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INVENTOR-INFORMATION:

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BEHRINGWERKE AG	DE

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INT-CL (IPC): A61L 25/00

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ABSTRACT:

1. Claims for the Contracting States : AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE A tissue adhesive containing, in liquid or solid form, fibrinogen, F XIII, a thrombin inhibitor, prothrombin factors and calcium ions and, where appropriate, a plasmin inhibitor. 1. Claims for the Contracting States : GR, ES A process for the production of a tissue adhesive, which comprises addition to an aqueous isotonic solution which has a pH of 7.5, which has been, where appropriate, pasteurized and, where appropriate, sterilized by filtration, and which contains at least 16 g/l human fibrinogen, 2 g-atoms of calcium per mol of fibrinogen and 1-6 g/l L-arginine monohydrochloride, of sufficient of a solution, which has, where appropriate, been pasteurized, of human factor XIII, of human albumin, of prothrombin concentrate, of antithrombin III and of aprotinin and, where appropriate, Na glutamate and isoleucine that the freeze-dried solution contains, in 1/4 of the volume dispensed into the container, these substances in the following concentration ranges : 65-115 mg/ml of human fibrinogen, 40-80 U/ml of factor XIII 4-40 mg/ml of human albumin, 1-50 IU/ml of PPSB (prothrombin factors), based on F II (prothrombin) 0.01-50 IU/ml of antithrombin III and, where appropriate, 1-10, 000 KIU of aprotinin/ml and 0-20 g/l of Na glutamate and 0-20 g/l of isoleucine.



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1. 1/19/1 (Item 1 from file: 345)

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Basic Patent (No,Kind,Date); AT 8200683 A 830915

PATENT FAMILY:

AUSTRIA (AT)

Patent (No,Kind,Date): AT 8200683 A 830915

VERFAHREN ZUR HERSTELLUNG EINES GEWEBEKLEBSTOFFES (German)

Patent Assignee: IMMUNO AG (AT)

Author (Inventor): LINDNER ADOLF DR; LINNAU YENDRA DR

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VERFAHREN ZUR HERSTELLUNG EINES GEWEBEKLEBSTOFFES (German)

Patent Assignee: IMMUNO AG (AT)

Author (Inventor): LINDNER ADOLF DR; LINNAU YENDRA DR

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immune complexes of patients with systemic lupus erythematosus are removed from blood by a filter contg. polymer absorbents. Thus, triallyl isocyanurate-vinyl acetate-vinyl ac. copolymer [81273-18-9] was synthesized, and L-tryptophan was immobilized on the surface of this polymer. This absorbent was packed in a cylinder and placed in an extracorporeal circulation of patients with systemic lupus erythematosus. The efficacy of the absorbent in removing immune complexes was demonstrated.

101: 78888u **Surgical threads.** Ethicon, Inc. Jpn. Kokai Tokkyo Koho JP 59 34,264 [84 34,264] (Cl. A61L17/00), 24 Feb 1984, US Appl. 401,661, 26 Jul 1982; 30 pp. Surgical threads are prep'd. from hydrophobic, thermally plasticized elastomers. These threads, when used in surgery, maintain mech. strength for a long time in the body. For example, poly[tetramethylene terephthalate-copoly(oxetetramethylene terephthalate)] [9078-71-1] was prep'd. from polymn. of di-Me terephthalate, 1,4-butanediol, and poly(tetramethylene oxide). The polymer was made into fibers and combined with silk to form a conjugated surgical thread.

101: 78889v **Lubricants for surgical rubber gloves.** James, Michael Howard; Bratby, David Michael; Blackley, David Charles; Duck, Roger; Poddell, Howard Irwin; Goldstein, Albert (LRC Products Ltd.) PCT Int. Appl. WO 84 00,908 (Cl. B21H21/04), 15 Mar 1984, GB Appl. 82/25,200, 09 Sep 1982; 27 pp. A skin-contacting lubricant layer formed from a hydrogel polymer bonded to a surgical rubber glove is treated with a bactericidal surfactant or a long chain fatty amine to improve the lubricity of the layer with respect to skin. A thin dipped surgical glove of natural rubber latex was leached with H₂SO₄, rinsed, primed by dipping in Al₂(SO₄)₃ soln., dried and dipped in 4% alc. soln. of 2-hydroxyethyl methacrylate-methacrylic acid copolymer [31693-08-0] followed by drying. The rubber was vulcanized and the lubricity with respect to dry skin was evaluated. The coating adhered satisfactorily to the rubber and no visible flaking was obse.

101: 78890p **Hydrogel contact lenses.** Atkinson, Ivor B.; Holdstock, Barry C.; Knowlton, John L. (CooperVision (U.K.) Ltd.) Eur. Pat. Appl. EP 106,650 (Cl. C08F226/10), 25 Apr 1984, GB Appl. 82/28,965, 11 Oct 1982; 17 pp. A soft hydrogel contact lens is formed from a hydrated lightly crosslinked copolymer of N-vinyl-pyrrolidone (NVP) and a short chain alkyl acrylate or methacrylate in a wt. ratio of 1.75-2.25 : 1, a short chain unsatd. carboxylic acid, a crosslinking monomer and a chem. free radical initiator. The lens has a high water content with good mech. propertics. Lenses were cut by lathing buttons prep'd. polymn. of redistd. methacrylic acid 3.22, purified Me methacrylate 32.18, NVP 64.37, and allyl methacrylate 0.23 g using AIBN as initiator. The lenses, hydrated by soaking in NaHCO₃ saline soln. at pH 7.4 had a hydrated refractive index of 1.376 and water content 73.4% wt./wt.

101: 78891q **Poly(vinyl alcohol) hydrogels as prosthetics.** Nippon Oil Co., Ltd. Jpn. Kokai Tokkyo Koho JP 59 56,446 [84 56,446] (Cl. C08L29/04), 31 Mar 1984, Appl. 82/164,870, 24 Sep 1982; 11 pp. A poly(vinyl alc.) [9002-89-8] aq. soln. is frozen and thawed repeatedly to obtain hydrogels that may be used as prosthetic materials. Thus, poly(vinyl alc.) with av. d.p. of >700 was dissolved in H₂O >6 wt. %, frozen at <-3°, thawed at <55°, and subjected to the freeze-thaw process repeatedly to obtain a hydrogel with greater mech. strength. The product was used as a substitute of femur articular cartilage in rabbits.

101: 78892r **Wound covering textile.** Braun, Karl Otto, K.-G. Austrian AT 374,361 (Cl. A61F13/00), 10 Apr 1984, Appl. 82/1,511, 19 Apr 1982; 7 pp. A wound covering that does not adhere to the skin and allows rapid removal of secretions from the wound surface is prep'd. from a highly elastic web of hydrophobic synthetic fibers (such as polyester, polyamide, and polypropylene) composing the wound contact surface. This surface is heat-treated to bond the fibers to each other and to an absorbent layer of highly napped fibers (such as cotton, cellulose, and linen).

101: 78893s **Hemostatic wound covering adhesive.** Lindner, Adolf; Linnau, Yendra (Immuno A.-G. fuer Chemisch-Medizinische Produkte) Austrian AT 374,367 (Cl. A61L15/04), 10 Apr 1984, Appl. 82/683, 23 Feb 1982; 4 pp. An adhesive dressing contains fibrinogen, blood-coagulation factor XIII [9013-56-3], a plasmin inhibitor, an antibiotic, and a cytostatic agent in a tissue-compatible protein or polysaccharide fleece or film matrix. Thus, 10 L frozen human plasma was warmed to 2° and the cryoppt. was obtained and sepd. from the cold-sol. proteins by extn. of the latter with buffer. The residue was dissolved in 100 mL citrate-glycine buffer at 37°, mixed with 2500 units aprotinin [9087-70-1], 20 IU heparin [9006-49-6], and 2000 mg amikacin sulfate [29831-55-5], and sterilized by filtration. The filtrate (contg. ≥1000 units factor XIII and ≥7500 mg fibrinogen) was used to treat 70 cm² pieces of collagen fleece (15 mL/piece), and the material was frozen, lyophilized, and packaged aseptically.

101: 78894t **Improved surgical dressings.** Nippon Kayaku Co., Ltd. Teikoku Selyaku Co., Ltd. Jpn. Kokai Tokkyo Koho JP 59 53,411 [84 53,411] (Cl. A61K9/70), 28 Mar 1984, Appl. 82/162,287, 20 Sep 1982; 4 pp. Improved surgical dressings comprise kaolin 1-10, urea [57-13-6] 0.8-2.0, gelatin 0.5-6.0, CM-cellulose Na [9004-32-4] 0.2-3.0, poly(Na acrylate) [25549-84-2] 6.0-10.0, polyhydric alc. 10.0-40.0, oils 0-6.0, surfactants 0-6.0, and H₂O to 100% by wt. The dressings have adequate adheasiveness, flexibility, and stabilizing effects on drugs incorporated. Thus, one dressing comprises kaolin 5, urea 1, gelatin 2, Me salicylate [119-38-8] 2, di-camphor 0.5, 1-menthol 0.625, ZnPO₄ 1, glycerin 20, poly(Na acrylate) 7.2, CM cellulose Na 1, and H₂O 59.675 parts.

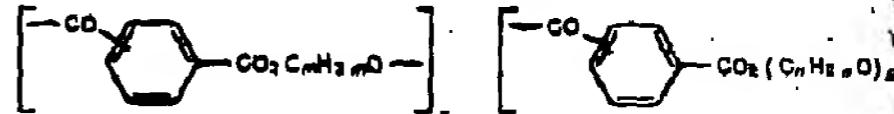
101: 78895u **Bandages for athletes.** Nitto Electric Industrial Co., Ltd. Jpn. Kokai Tokkyo Koho JP 59 51,855 [84 51,855] (Cl.

A61L15/06), 26 Mar 1984, Appl. 82/162,930, 18 Sep 1982; 20 pp. Bandages for the protection of skin and muscles against injury and destr. athletes are prep'd. using polyester-cotton cloths treated with water-repellents and adhesives. Thus, a cloth contg. polyester and cotton mixed fibers (30:70%) for the warp and cotton fibers for the weft. Part of the cloth is treated with a water-repellent, octadecyl isocyanate-vinyl ac. copolymer [91310-21-3], on one side, and treated on the other with a rubber pressure-sensitive adhesive comprising natural rubber 100, a rosin 100, zinc White 100, polybutene 20, and a preservative 1 part. Improved phys. properties of this bandage were described.

101: 78896v **Individual dental castings.** Pfannenstiel, Hans-Joachim; Huebner, Heijo (ESPE Fabrik Pharmazeutischer Produkte GmbH) Ger. Offen. DE 3,240,907 (Cl. B22C1/22), 10 May 1982, Appl. 05 Nov 1982; 20 pp. Individual dental castings are prep'd. from a photopolymerizable mass contg. an acrylate or a methacrylate monomer, a photoinitiator such as camphorquinone and photoinitiator, the mass at 400-500 nm. Form-stable casting models for the form of crowns, bridges, inlays and secondary parts for dentures can be built by using this method. Thus, a mixt. of 1 part bis-GMA and 1 part of triglycol dimethacrylate contg. 1% camphorquinone and 1.5% triethanolamine is polymed. with light. When the casting model is finished, it is taken out of the cavity, a casting canal prep'd. earlier from wax is attached to the casting model and the whole product is embedded in a fire-damp. plastic mass. The mass is heated to 600° and the casting is burnt free from residues and finally, a liq. metal such as Au is poured into the casting form. After cooling the model is taken out and give a precise Au inlay.

101: 78897w **Activated carbon products for surgical dressings.** Maggs, Frederick Arthur Pomroy (Charcoal Cloth Ltd.) Brit. Pat. Appl. GB 2,127,389 (Cl. C01B31/08), 11 Apr 1984, GB Appl. 82/26,028, 13 Sep 1982; 4 pp. An activated C product (charcoal cloth or felt) contains Zn, Al, Ca, Mg or Fe, which is dispersed in it and may be used in surgical dressings, particularly when it contains Ag. Thus, an impregnation soln. was prep'd. NH₄Cl, ZnCl₂ 9, AlCl₃ 9, citric acid [77-92-9] 4, NH₃ 5 and H₂O 0.2%. Three lengths of rayon cloth (25 × 5 cm) were dipped in a shallow trough contg. the impregnation soln. and each length passed through roller nips at 345 kPa and plant oven-dried at 100° b single pass. Samples were charred at 360° in CO₂ following activation in C₂ at 950°. The cloth was active against *Staphylococcus aureus* and other bacteria.

101: 78898x **Polymers for surgical goods.** Terumo Corp. Kokai Tokkyo Koho JP 59 68,364 [84 68,364] (Cl. C08L27/20), 24 Apr 1984, Appl. 82/178,050, 09 Oct 1982; 6 pp. Surgical



prep'd. from halogenated vinyl polymer and I (x:y = 3:1-20:1; m = 2-20; p = 5-50) have improved biocompatibility. Thus, I (9:1; m = 3; n = 2-10; p = 9; mol. wt. 45,000) and PVC (9002-4) (mol. wt. 42,000) were mixed at 75:25, heated up to 130°, and into sheets (thickness, 0.4 mm). Phys., chem., and biol. properties of the sheet were studied. The sheet may be used for the prep. blood bag and clin. tubes.

101: 78899y **Hydrogel contact lenses for permanent wear.** Atkinson, Ivor B.; Holdstock, Barry C. U.S. US 4,451,636 (Cl. C08F26-261; C08F26/06), 29 May 1984, GB Appl. 83/11,788, 29 Jun 1983; 4 pp. Hydrogel contact lenses having high tensile and adhesion properties are prep'd. from hydroxy alkyl(meth)acrylate copolymers contg. a triazine deriv. crosslinking agent. The compn. contg. N-vinylpyrrolidone 30, hydroxyethyl methacrylate 89.22, methacrylic acid 0.42, 1,3,5-tris(propenoxy)-2,4,6-triazine 0.3, and ethylene glycol dimethacrylate 0.08% were mixed with 0.2% of a monomer of azobisisobutyronitrile. The mixt. was cast in a mold. and polymed. to give lens blanks and swelled with a mild alk. to 100% to a saline soln. The resulting copolymer [91293-21-9] hydrogel had tensile strength 2.75 Kgf/cm² and tear strength 0.296 Kgf/cm² after initiation.

101: 78900z **Filling material for teeth.** Makarov, K. A.; Shitov, M. Z.; Karal'nik, D. M.; Batovskii, V. N.; Dovgopol, V. N.; Sorokina, T. G.; Alekseeva, L. S.; Gagarina, L. M. (Lenmedizdat) Medical Institute; Kharkov Plant of Medical Plastics and Materials) U.S.S.R. SU 1,088,726 (Cl. A61K6/02), 30 Apr 1983, Appl. 3,654,103, 15 Feb 1983. From Otkrytiya, Izobret., 1983, No. 10/04, 1983; 4 pp. Hydrogel contact lenses having high tensile and adhesion properties are prep'd. from hydroxy alkyl(meth)acrylate copolymers contg. a triazine deriv. crosslinking agent. The compn. contg. N-vinylpyrrolidone 30, hydroxyethyl methacrylate 89.22, methacrylic acid 0.42, 1,3,5-tris(propenoxy)-2,4,6-triazine 0.3, and ethylene glycol dimethacrylate 0.08% were mixed with 0.2% of a monomer of azobisisobutyronitrile. The mixt. was cast in a mold. and polymed. to give lens blanks and swelled with a mild alk. to 100% to a saline soln. The resulting copolymer [91293-21-9] hydrogel had tensile strength 2.75 Kgf/cm² and tear strength 0.296 Kgf/cm² after initiation.

101: 78900s **Filling material for teeth.** Makarov, K. A.; Shitov, M. Z.; Karal'nik, D. M.; Batovskii, V. N.; Dovgopol, V. N.; Sorokina, T. G.; Alekseeva, L. S.; Gagarina, L. M. (Lenmedizdat) Medical Institute; Kharkov Plant of Medical Plastics and Materials) U.S.S.R. SU 1,088,726 (Cl. A61K6/02), 30 Apr 1983, Appl. 3,654,103, 15 Feb 1983. From Otkrytiya, Izobret., 1983, No. 10/04, 1983; 4 pp. Hydrogel contact lenses having high tensile and adhesion properties are prep'd. from hydroxy alkyl(meth)acrylate copolymers contg. a triazine deriv. crosslinking agent. The compn. contg. N-vinylpyrrolidone 30, hydroxyethyl methacrylate 89.22, methacrylic acid 0.42, 1,3,5-tris(propenoxy)-2,4,6-triazine 0.3, and ethylene glycol dimethacrylate 0.08% were mixed with 0.2% of a monomer of azobisisobutyronitrile. The mixt. was cast in a mold. and polymed. to give lens blanks and swelled with a mild alk. to 100% to a saline soln. The resulting copolymer [91293-21-9] hydrogel had tensile strength 2.75 Kgf/cm² and tear strength 0.296 Kgf/cm² after initiation.

101: 78901t **Sterilizing with hydrogen peroxide and neutralizing a residual amount thereof.** Housby, Robert Dennis (CooperVision Inc.) Eur. Pat. Appl. EP 110,809 (Cl. A01N59/00), 13 Jun 1984, US Appl. 444,045, 23 Nov 1982; 23 pp. Surfaces and devices, thermal contact lenses sterilized with aq. H₂O₂ soln. are treated with aq. pyruvate [113-24-6] soln. to decompose the residual H₂O₂. The removal of H₂O₂ from the devices makes them nonirritating to intact tissues. Thus, a neutralizing soln. contained Poloxamer 407, NaCl 0.2, KCl 0.1, sorbic acid 0.2, Na borate 0.22, di-Na edetate, added boric acid 1.0, and Na pyruvate 0.5% and purified water sufficient amt. Eight lenses were soaked in 3% H₂O₂ for 10 min, then cult. in a nutrient broth. Neither lens showed growth, indicating